

AMENDMENTS TO THE CLAIMS

This listing of the claims replaces all prior listings and versions:

1. (withdrawn and currently amended): A method of selecting a switching system, the switching system comprising ~~(i) a first component comprising a first polypeptide and (ii) a second component comprising a second polypeptide, in which the first polypeptide binds to the second polypeptide in a manner modulatable by a ligand, and (iii) a third component comprising the ligand, wherein the first and second polypeptides bind to DNA, wherein the first or second polypeptide comprises a Cys2-His2 zinc finger protein;~~

(a) a heterodimer comprising

(i) a first polypeptide, and

(ii) a second polypeptide; and

(b) a ligand;

wherein the first and second polypeptides bind to DNA, and further wherein the first or second polypeptide comprises an engineered Cys2-His2 zinc finger binding domain;

the method comprising the steps of:

(a) contacting one or more ~~candidate~~ first polypeptides with one or more ~~candidate~~ second polypeptides in the presence of one or more ligands,

(b) selecting a complex ~~of the~~ comprising a first polypeptide component, a second polypeptide component and a ligand component ~~three components;~~

(c) optionally isolating and/or identifying the an unknown components component ~~of the complex;~~

(d) comparing the binding of the first polypeptide ~~component of the complex~~ to the second polypeptide ~~component of the complex~~ in the presence and absence of the ligand ~~component of the complex;~~ and

(e) selecting one or more complexes where said binding differs in the presence and absence of the ligand ~~component,~~

in which at least one of the first polypeptide, second polypeptide or ligand ~~component~~ is provided in the form of a library of members.

2. (withdrawn and currently amended): A method according to Claim 1, in which ~~at least one of the candidate~~ first polypeptide[[s]] ~~comprises a non-naturally occurring binding domain which~~ binds to the second polypeptide.

3. (canceled)

4. (withdrawn): A method according to Claim 1, in which one or both of the first and second polypeptides is provided as a plurality of molecules.

5. (withdrawn): A method according to Claim 4, in which the plurality of molecules is a library.

6. (canceled).

7. (withdrawn and currently amended): A method according to ~~Claim 4~~ claim 1, in which ~~one of the components~~ the component isolated and/or identified in step (c) is a the ligand component.

8. (withdrawn and currently amended): A method according to ~~claim 4~~ claim 1, in which ~~one of the components~~ the component isolated and/or identified in step (c) is a polypeptide that binds to DNA.

9. (canceled).

10. (withdrawn): A method according to claim 4, in which a plurality of candidate ligands are used.

11. (withdrawn): A method according to claim 4, in which the ligands are provided as a library of ligands.

12. (canceled).

13. (withdrawn): A method according to claim 1, in which one or both of the first or second polypeptides are transcription factors.

14. (withdrawn): A method according to claim 13, in which the transcription factor is a zinc finger transcription factor.

15. (withdrawn): A method according to claim 1, in which one or both of the first or second polypeptides are provided as a phage display library.

16 through 20. (canceled).

21. (withdrawn and currently amended): A method of modulating the expression of one or more genes, said method comprising administering a switching system ~~and a ligand~~ selected according to the method of claim 1 to a cell, in which ~~the~~ regulatory sequences of the genes comprise a target nucleic acid sequence.

22. (withdrawn and currently amended): A method of modulating the expression of one or more nucleotide sequences of interest in a host cell which host cell comprises a nucleic acid sequence capable of directing the expression of the first and second polypeptides ~~a switching system~~ selected according to the method of claim 1 and a target nucleic acid sequence to which the ~~switching system~~ complex binds in a manner modulatable by a ligand, which method comprises administering said ligand to the cell ~~and wherein the switching system is heterologous to the host cell~~.

23. (withdrawn): A method according to Claim 21 wherein the host cell is a plant cell.

24. (withdrawn and currently amended): A method according to Claim 23, in which the plant cell is part of a plant and ~~the target sequence is part of a~~ the regulatory sequence ~~is to which the nucleotide sequence of interest is operably linked, said regulatory sequence being~~ preferentially active in the male or female organs of the plant.

25. (withdrawn): A non human transgenic organism comprising a target nucleic acid sequence and a nucleic acid sequence capable of directing the expression of a nucleic acid binding molecule which binds to the target nucleic acid in a manner

modulatable by a ligand, in which the target nucleic acid sequence and/or nucleic acid sequence are heterologous to the organism.

26. (withdrawn): A transgenic non-human organism according to Claim 25 which is a plant.

27 to 30. (canceled).

31. (withdrawn): A method according to claim 1, in which the ligand is an immunoglobulin molecule, preferably an antibody molecule.

32 to 33. (canceled)

34. (currently amended): A complex comprising

(a) a heterodimer comprising

(i) a first polypeptide, and

(ii) a second polypeptide; and

(b) a ligand,

~~switching system comprising a protein switch comprising: (i) a first component comprising a first polypeptide and (ii) a second component comprising a second polypeptide, in which the first polypeptide binds to the second polypeptide in a manner modulatable by a ligand, and (iii) a third component comprising the ligand, wherein the first and second polypeptides bind to DNA, and further wherein the first or second polypeptide comprises a non-naturally occurring~~ an engineered Cys2-His2 zinc finger binding domain.

35. (withdrawn and currently amended): A method of regulating transcription from a nucleic acid sequence comprising providing a target nucleic acid to which a ~~switching system~~ complex according to claim 34 binds and binding the ~~switching system~~ complex to the target nucleic acid, thereby regulating transcription.

36 and 37. (canceled).

38. (withdrawn and currently amended): A method of modulating the expression of one or more genes, said method comprising administering a ~~switching-system~~ complex according to Claim 34 to a cell, in which the regulatory sequences of the genes comprise a target nucleic acid to which the ~~switching-system~~ complex binds in a manner modulatable by the ligand.

39. (withdrawn and currently amended): A method of modulating the expression of one or more nucleotide sequences of interest in a host cell which host cell comprises a first nucleic acid sequence capable of directing the expression of the first polypeptide of the ~~switching-system~~ complex according to Claim 34, a second nucleic acid sequence capable of directing the expression of the second polypeptide of the ~~switching-system~~ complex according to Claim 34, and a target nucleic acid sequence to which the ~~at least one of the first or second polypeptides of the switching-system~~ complex binds, which method comprises administering said ligand to the cell such that the complex is formed.

40. (withdrawn and currently amended): A method according to Claim 39, in which the at least one DNA-binding polypeptide component of the ~~switching-system~~ complex is heterologous to the host cell.

41. (withdrawn): A method according to Claim 39 wherein the host cell is a plant cell.

42. (withdrawn): A method according to Claim 41, in which the plant cell is part of a plant and the target sequence is part of a regulatory sequence to which the nucleotide sequence of interest is operably linked, said regulatory sequence being preferentially active in the male or female organs of the plant.

43. (withdrawn): A non human transgenic organism comprising a target nucleic acid sequence, a first nucleic acid sequence capable of directing the expression of a nucleic acid binding protein, and a second nucleic acid sequence capable of directing the expression of a second polypeptide which binds to the nucleic acid binding protein in a manner modulatable by a ligand, in which the nucleic acid binding protein binds to the

target nucleic acid sequence in a manner modulatable by binding of the second polypeptide.

44. (withdrawn): An organism according to Claim 43, in which any or all of the first nucleic acid sequence, the second nucleic acid sequence, and the target nucleic acid sequence are heterologous to the organism.

45. (withdrawn): A transgenic nonhuman organism according to Claim 43 which is a plant.

46. (withdrawn and currently amended): A method according to claim 1, in which the first polypeptide ~~component of the complex~~ has a higher affinity for the second polypeptide ~~component of the complex~~ in the presence of the ligand ~~component~~ than in the absence of the ligand ~~component~~.

47. (withdrawn and currently amended): A method according to claim 1, in which the first polypeptide ~~component of the complex~~ has a higher affinity for the second polypeptide ~~component of the complex~~ in the absence of the ligand ~~component~~ than in the presence of the ligand ~~component~~.

48. (currently amended): A switching system comprising a protein switch comprising: (i) a first component comprising a first polypeptide and (ii) a second component comprising a second polypeptide, in which the first polypeptide binds to the second polypeptide in a manner modulatable by a ligand, and (iii) a third component comprising the ligand, wherein the first and second polypeptides bind to DNA, and further wherein the first or second polypeptide comprises an engineered Cys2-His2 zinc finger binding domain.

49. (canceled).